THE LEUCOCYTES IN CROUPOUS PNEUMONIA.

By John S. Billings, Jr., *Assistant Resident Physician, Johns Hopkins Hospital.*

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The increase in the number of leucocytes in the blood in croupous pneumonia may be said to have been first noticed by Piorry[1] in 1839. He remarked that the so-called "crusta phlogistica," seen above the clotted blood withdrawn by venesection from patients suffering from any of the acute inflammatory diseases, was most marked in pneumonia. It was thickest at about the seventh or eighth day, just before the crisis, and he thought it to be due to an hæmitis or an actual inflammation of the blood itself.

Virchow[2] in 1871 spoke of a leucocytosis in pneumonia and held that there was an actual new formation of leucocytes, *i. e.* an absolute increase in the total number present in the circulation, but only in those cases in which there was swelling of the bronchial glands.

Since then there have been many investigations on the subject, especially in the last four years. Nasse,[3] Koblanck, Sörensen and Pée all noted the presence of a leucocytosis during the course of croupous pneumonia, but they did not speak of its relation to the temperature, nor to prognosis.

Halla[4] in 1883 was the first to report a series of cases, fourteen in number. In twelve of these there was a leucocytosis, while in the remaining two the leucocytes were not increased. Both the latter cases ended fatally. He was the first to call attention to the fact that the absence of leucocytosis is of bad omen. He found no correspondence between the temperature and leucocyte curves in those cases ending in recovery.

Hayem and Gilbert[5] in 1884 remarked upon the typhoid character of those cases of pneumonia in which there is no leucocytosis.

Tumas[6] in 1887 stated that there was a rough daily correspondence between the temperature and the leucocytes, and that

the number of the latter was greatest at the severest stages of the disease. He also noted that the leucocytes did not reach normal at the same time as the temperature, but remained elevated for three or four days after the crisis.

Boekmann[7] and Von Jaksch[8] claim that there is a constant relation between the number of leucocytes and the temperature in various acute infectious diseases, and particularly in pneumonia.

Kikodse[9] states that leucocytosis is absent only in fatal cases. He believes that the leucocytosis begins before the involvement of the lung takes place, that it runs parallel with the temperature, and falls to a point below normal with the crisis in temperature.

Roemer[10] believes the eucocytosis in pneumonia to be caused by the products of destruction (bacteria, cells, etc.) brought about by the alkali-proteins, and not directly by the alkali-proteins themselves.

Von Jaksch,[11] recognizing the bad prognosis in cases which showed no leucocytosis, and believing that the fatal termination was due directly to its absence, recommended the use of drugs which would produce an increase in the number of leucocytes in the blood. (Antipyrin, pilocarpin, etc.) Such treatment was ineffectual, as will be demonstrated later.

Maragliano[12] does not think that the number of leucocytes is of any prognostic value.

Rieder[13] reports his observations in twenty-six cases. He finds that the fall of the leucocytes generally precedes the fall of temperature, but that the number of the leucocytes, while beginning to fall first, may often remain elevated for several days after the temperature has touched normal. This is particularly marked in cases of delayed resolution. In cases ending by lysis the leucocytes fall correspondingly slowly. A pseudo-crisis may be recognized by the fact that while the temperature may fall to normal, the leucocytes remain steadily elevated. He finds no correspondence of the leucocyte and temperature curves. The leucocytosis was present in one case six hours after the chill. In fatal cases there was no leucocytosis, but the blood showed the characteristic change noted in so-called pure leucocytoses, *i. e.*, a marked relative increase in the number of so-called polynuclear elements. He does

not think there is any relation between the amount of leucocytosis and extent of lung involved.

V. Limbeck[14] holds that only those infectious diseases with exudation into the tissues show an increase in number of the leucocytes. The amount of leucocytosis depends upon the quality and quantity of the exudate, *i. e.*, the more cells and the larger the exudate, the greater the leucocytosis. He states that in pneumonia the leucocytosis disappears with the fever. Should there be a new extension of the disease and a rise of fever, the leucocytosis reappears a few hours before the rise in temperature takes place. A pseudo-crisis may be recognized by a steady leucocytosis. A fatal ending is foreshadowed by a steady rise in the number of the leucocytes.

Tchistovitch[15] inoculated rabbits with cultures of pneumococcus and found a leucocytosis only in those cases ending in recovery. The use of stronger cultures which killed the animal did not cause any leucocytosis, but brought about an actual reduction in the number of the leucocytes, *i. e.*, a so-called leukolysis. This was confirmed by Rieder (l. c.).

Laehr[16] reports observations of the leucocytes in sixteen cases of pneumonia. He found the leucocytosis in one case to be present eight hours after the chill. The leucocytes rise one to two days before the crisis, to sink again before the crisis takes place. The temperature reaches normal before the leucocytes. He finds no exact correspondence between the number of leucocytes, the fever and the amount of lung involved, but thinks they do correspond roughly. He believes the leucocytosis to be due to chemotaxis, the attracting substances being the alkali-proteins, etc., produced by the pneumococcus. Persistence of the leucocytosis signifies delayed resolution of the pneumonic consolidation, and its reappearance indicates a recurrence of the disease.

Schulz[17] states that the leucocytosis observed in pneumonia, as well as all other inflammatory leucocytoses, is not due to any absolute increase in the number of leucocytes in the circulation, but only an altered division. He believes that in health the large abdominal vessels contain many more leucocytes ("Wandständig") than the peripheral vessels. In disease the presence of abnormal chemotactic substances in the blood, and the increased rapidity and force of the respiration and

circulation, are enough to drive these extra leucocytes out into the circulation and to those points where they may be needed.

Rovighi[18] states that in pneumonia the leucocytes reach their highest point during the period of fall of temperature. He bases this statement on the results of experiments going to show that when the body is heated the number of leucocytes in the peripheral circulation diminishes, while cooling the body increases their number. These are purely local phenomena, not due in any way to changes on the part of the blood-making organs.

Cabot[19] reports observations in seventy-two cases of pneumonia. Seven of these ended fatally, and six out of the seven showed no leucocytosis. In one case ending in recovery, which showed no leucocytosis at first, there was a steady rise in the number of the leucocytes towards the end of the disease. He does not think that there is any relation between the amount of leucocytosis, the degree of severity of the case, and amount of lung involved.

Ewing[20] reports a number of cases, and draws the following conclusions. 1. The greater the amount of lung involved, the greater the leucocytosis. 2. The amount of leucocytosis corresponds to the "systemic reaction," the latter being judged by the temperature, pulse and general condition of the patient: *i. e.*, in fatal cases there is no leucocytosis, and *vice versa.* 3. A well marked leucocytosis indicates a severe infection, a low leucocytosis is unfavorable, and the absence of any leucocytosis makes the prognosis very grave.

Tchistovitch[21] reports the results of some further inoculation experiments upon animals. As is well known, the inoculation of animals with certain substances (tuberculin, sterile culture of staph. py. aur., and pilocarpin) produces first a temporary leukolysis (so-called), which is followed by a marked leucocytosis. He found that those substances which produce a leucocytosis in healthy rabbits do not do so when injected into rabbits previously inoculated with virulent cultures of pneumococcus. The progressive diminution of the leucocytes caused by the latter substance steadily continues, or at most there is only a slight transient leucocytosis, which is followed by a fresh fall. He holds this to show that those cases of pneumonia which succumb to the great viru-

lence of the specific pneumococcus, should show no leucocytosis, and that no stimulant of leucocytosis should be able to produce any leucocytosis in such cases. So that the presence of a leucocytosis in fatal cases of pneumonia should make us doubt that the virulence of the specific pneumococcus was the cause of death, and we should seek some other cause of death in such cases, such as extensive involvement of the lungs or localization of the disease in the heart or in the brain.

When he injected the pneumococcus culture into the brain of the animal there was produced a meningo-encephalitis with a marked rise in the number of leucocytes in the blood. The amount of culture used was just so much as, injected elsewhere in the body, would bring about a severe infection with leukolysis, but without fatal termination. In conclusion, he holds that the presence or absence of leucocytosis only shows the virulence of the poison and is not a criterion of absolute prognosis.

He saw four fatal cases of pneumonia. In one there was no leucocytosis. Of the other three, all of which showed a leucocytosis, one had endocarditis and meningitis, another meningitis, while the third case showed extensive consolidation of both lungs.

Bieganski[22] reports a series of cases, paying especial attention to the relative numerical proportions of the various forms of leucocytes. In cases showing a marked leucocytosis, 80 to 90 per cent. of the leucocytes are polynuclears, while the eosinophiles and blood-plates are practically absent. Just after the crisis in temperature the polynuclears sink to below 60 per cent., while the eosinophiles and blood-plates reappear in increased numbers, about three days being taken for the blood to return to its normal condition. In fatal cases the polynuclears are reduced to 50 per cent. or below. Such a condition of the blood together with an absence of leucocytosis makes the prognosis unfavorable.

He holds that the leucocytosis in pneumonia is due to a lessened destruction of the polynuclear forms. This is brought about by the toxines of bacterial origin which are circulating in the blood. The mononuclear elements are unaffected and continue to enter the circulation and to develop there into polynuclears. Here all progress ceases and there is neither

any destruction of the polynuclears with formation of blood plates, nor further development of the polynuclears into eosinophiles. In the fatal cases the toxines are supposed to have a paralyzing effect upon the development of all the forms of leucocytes, and also to prevent the entrance of young forms into the circulation.

The twenty-two cases here reported were not picked ones, excepting that eight or ten were thrown out, either because too few counts were made or because the crisis in temperature occurred within twenty-four hours after entry into hospital. The methods and precautions used in counting the blood, and in examining and preparing dried and stained specimens, were exactly the same as those employed in the investigations of the leucocytes in malarial fever reported by the writer in the October number of this journal for 1894.

In each case charts were made of the leucocyte and temperature curves, so that comparison of the two could readily be made. Three of these charts are reproduced in this article. The leucocytes were counted on an average of twice a day during the febrile period.

Cases.

1. W. R., æt. 26. Illness lasted 12 days. Right middle, right lower and left lower lobes involved. Temperature ranged high until sixth day, when it fell by lysis, taking 6 days to reach normal. Leucocytes 39,500 six hours after chill. No daily correspondence with temperature curve; they reached their highest point (50,000) two hours after temperature began to fall. Thenceforth they fell steadily, reaching normal one day after temperature.

2. S. F., æt. 51. Illness lasted 8 days. Right middle and lower lobes involved. Temperature ranged at 102° for 6 days; fell by lysis, reaching normal in 50 hours. Leucocytes 42,000 8 hours after chill. They fell steadily until temperature began to fall, when they rose sharply to 38,000, reaching normal 2 days after temperature.

3. H. H., æt. 22. Illness lasted 17 days. Right middle and lower lobes involved, with delayed resolution. Temperature fell on seventh day of disease, to rise again sharply to 102°. Fell again by lysis, reaching normal in 5 days. Leuco-

cytes ranged between 20,000 and 28,000 until the day the temperature touched normal, when they began to fall, reaching normal eleven days after temperature.

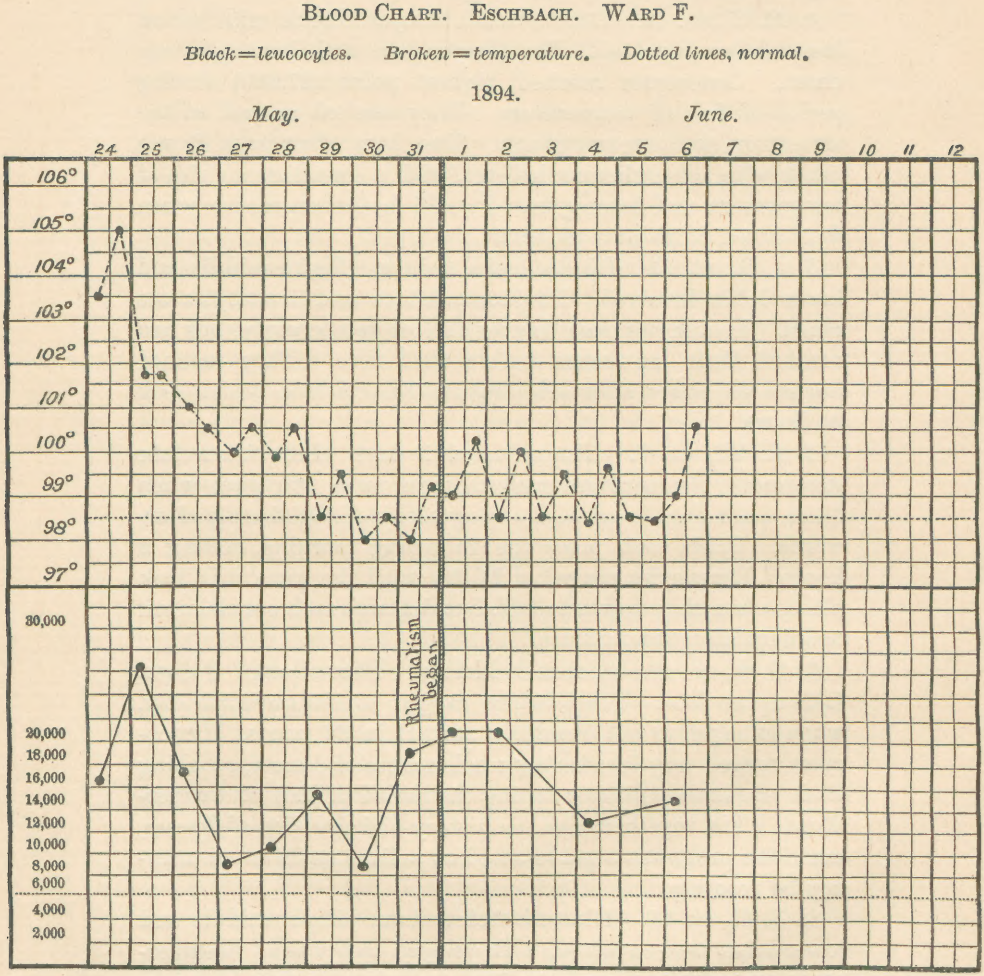
4. R. E., æt. 42. Illness lasted 9 days. Right middle and lower lobes involved. For temperature and leucocytes see chart. Leucocytes reached highest point (27,000) during period of fall of temperature. They reached normal at the same time as the temperature. Two days afterwards P. was taken with acute rheumatic fever, with a simultaneous rise of temperature and leucocytes. P. still had rheumatism when discharged at his own request.

5. J. S., æt. 13. Illness lasted 6 days. Right middle and lower lobes involved. For temperature and leucocytes see chart. Leucocytes rose during fall of temperature, but had reached their maximum before that time. They reached normal 36 hours after temperature, the crisis in which took 24 hours.

6. E. W., æt. 7. Illness lasted 9 days. Left lower lobe involved. Temperature ranged high until 8th day, when there was a pseudo-crisis, the temperature rising sharply afterwards. Crisis took place the following morning, lasting 2 hours. Leucocytes ranged at 24,000 until the true crisis took place, when they began to fall, but did not reach normal until two days after temperature.

7. G. S., æt. 40. Alcoholic history. Illness lasted 7 days. Left upper lobe. Temperature ranged at 105 until 5th day, when it began to fall, reaching normal in 36 hours. Leucocytes ranged very low during whole course of disease, reaching their maximum (13,000) during the period of fall of temperature. This, together with the history and situation of disease, made the prognosis a grave one, but patient made an uninterrupted recovery.

8. E. F., æt. 20. Illness lasted 8 days. Right middle and lower lobes were involved, with delayed resolution. Temperature ranged high until the 7th day, when it fell by crisis, reaching normal in 10 hours. Leucocytes ranged at about 25,000 until crisis in temperature, when there was a slight fall to 16,000, followed by a gradual rise to 27,000, the leucocytes not reaching normal until 7 days after temperature.

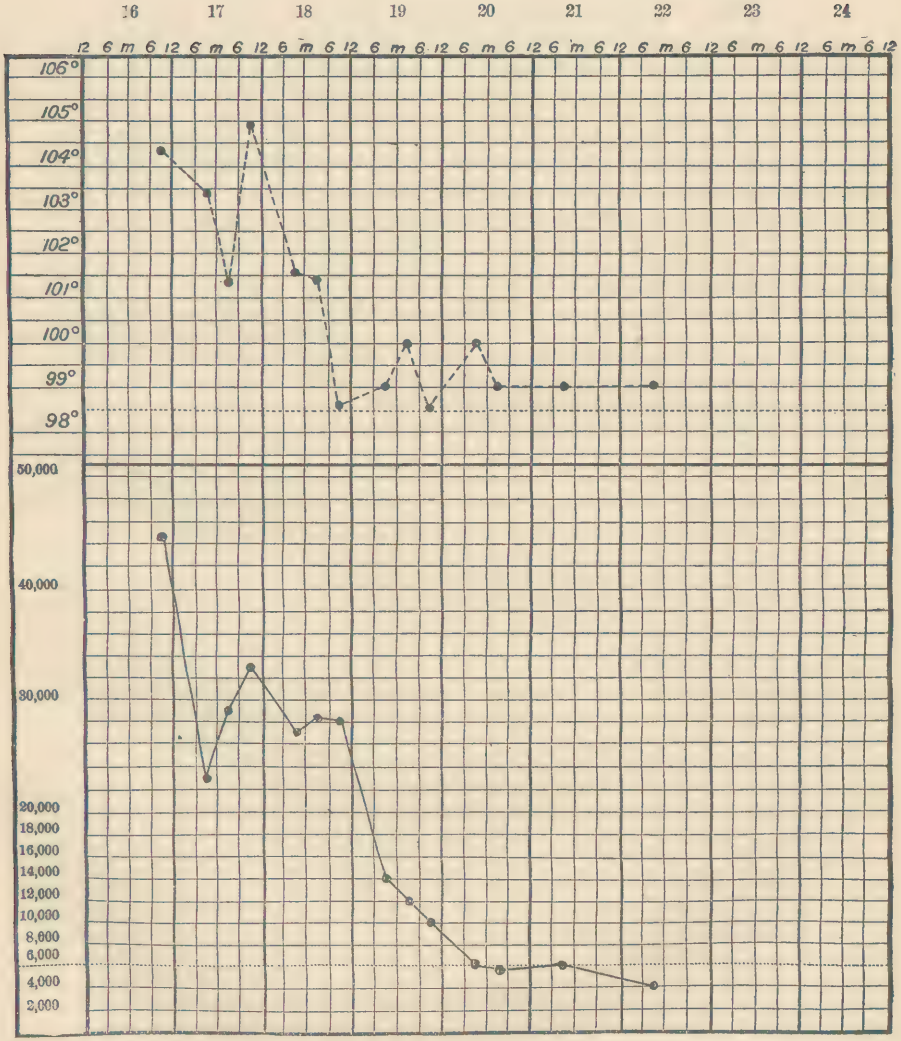


Case 4. Pneumonia and Rheumatic Fever. Showing fall by Lysis.

BLOOD CHART. SCHULTZ. WARD F.

Black = leucocytes. Broken = temperature. Dotted lines, normal.

February, 1893.



CASE 5. PNEUMONIA. SHOWING FALL BY CRISIS.

9. C. J., æt. 30. Patient was admitted for tertian malarial fever. Lungs were clear on admission, and the pneumonia began 36 hours later. For temperature and leucocytes see chart. Quinine was given on the evening of the chill, and the malarial organisms rapidly disappeared, and with their disappearance the number of leucocytes rapidly increased. There was successive involvement of the right lower, right middle and left lower lobes, each fresh extension of the disease being followed by a sharp rise in the number of the leucocytes. Leucocytes reached highest point (68,000) just before the fall in temperature began, and thenceforth decreased in number, reaching normal 6 days after temperature.

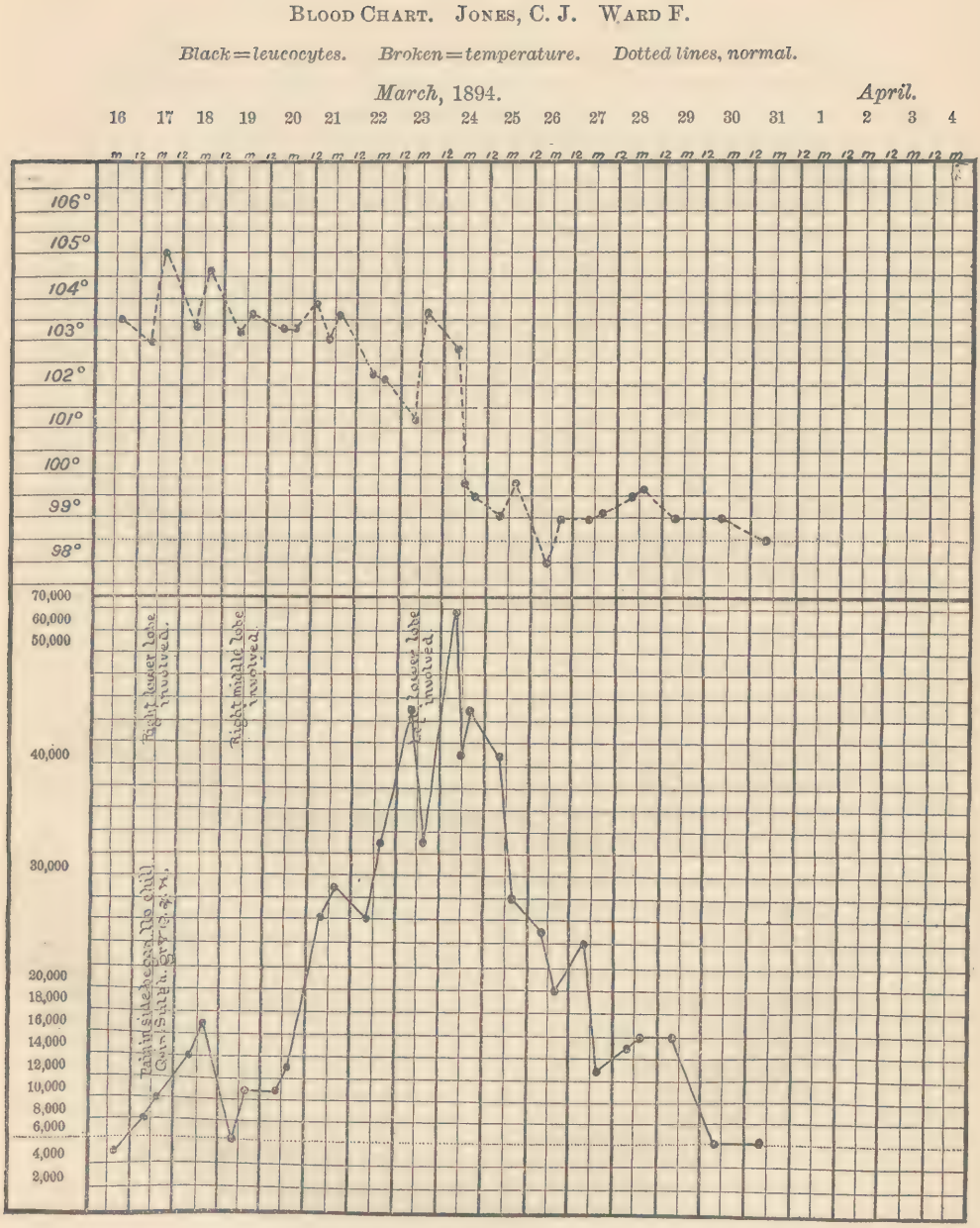
10. E. M., æt. 45. Illness lasted 10 days. Left upper lobe involved. Temperature ranged at 103° until 9th day, when it fell by crisis, reaching normal in 16 hours. Leucocytes reached maximum (36,000) two days before crisis. They fell with temperature, but did not reach normal until two days after crisis.

11. C., æt. 26. Illness lasted 13 days. Right upper, middle and lower lobes involved. Temperature ranged at 104° until 11th day, when it fell by crisis, reaching normal in 48 hours. Leucocytes low on admission; reached maximum (29,000) during period of fall of temperature. Did not reach normal until 7 days after temperature.

12. L. K., æt. 24. Illness lasted 8 days. Right lower lobe involved. Temperature ranged high until 8th day, when it fell to normal in 24 hours. Leucocytes ranged at 25,000 until crisis in temperature occurred, when they fell to 16,000, but rose again to 29,000 (maximum). They did not reach normal until 8 days after temperature. Delayed resolution.

13. J. H., æt. 41. Illness lasted 10 days. Right upper lobe involved. Temperature ranged between 102° and 104° until day of death, when it fell, being 100° 2 hours before death. Leucocytes 22,000 on admission, rose to 38,000 that p. m., falling steadily afterwards. 10,000 just before death. No autopsy.

14. J. W., æt. 73. Illness lasted 8 days. Right upper, middle and lower lobes involved. Temperature ranged at 101° until 30 hours before death, when it rose to 104°. Leucocytes ranged at 25,000 from admission until death. Autopsy.



Case 9. Pneumonia and Malaria. Showing fall by Crisis.

In addition to pneumonic consolidation above noted, P. had an acute fibrino-purulent meningitis due to the dip. pneumoniæ.

15. G. W., æt. 25. Illness lasted 10 days. Right upper, middle and lower and left lower lobes involved. Temperature ranged from 101.5° to 104°, being 104.2° at death. Leucocytes 8,000 on admission, rose steadily until time of death 8 days later, when they were 30,000. Autopsy showed the pneumonic consolidation above noted. No meningitis nor endocarditis.

16. K. D., æt. 47. Illness lasted 4 days. Right upper and middle lobes involved. Temperature ranged at 102.5° until death, with a pseudo-crisis to 99° 12 hours before death. Leucocytes 18,000 on admission, where they ranged until death. 15,000 just before death. No autopsy.

17. C. L., æt. 36. Illness lasted 21 days (?). Lower lobes of both lungs involved. Temperature ranged steadily at 102° until 12 hours before death, when there was a pseudo-crisis to 99°, with a sharp rise to 103° just before death. Leucocytes 13,000 on admission, fell gradually to normal in two days. They began to rise 36 hours before death, reaching 32,000 just before the end. No autopsy.

18. J. C., æt. 63. Illness lasted 11 days. Right middle and lower lobes involved. Temperature ranged at 103.5° until 2 days before death, when it rose to 106.2°, falling to 104° just before death. Leucocytes 8,000 on admission. Remained normal until day before death, when they rose to 20,000, falling to 14,000 before death. No autopsy.

19. F. S., æt. 50. History of alcoholism. Illness lasted 24 days (?). Right upper and middle lobes involved. Temperature ranged at 104° during the four days preceding death. The afternoon of the fourth day the P., being left alone for a moment, climbed through the top of a window and fell to the ground outside, breaking vertebral column and both bones of right leg. Unsatisfactory coroner's inquest showed nothing beyond the fractures and the pneumonic consolidation above noted. Leucocytes 15,000 on admission; for the first 3 days fell gradually to 11,000, but after the accident above referred to, rose to 18,000. P. lived 4 hours after the accident occurred.

20. H. L., æt. 41. Illness lasted 5 days. Right lower base involved. Temperature on admission 102.5°. For next three days it ranged at 104°, being 103.8° just before death. Leucocytes 10,000 on admission, after which time they ranged steadily below normal; from 6,000 to 1,500. They were 4,000 just before death. No autopsy.

21. A. N., æt. 47. Illness lasted 12 days. Lower lobes of both lungs involved. Temperature ranged from 103.5°–105°, until shortly before death, when it rose to 107°. Leucocytes 15,000 on admission; 2 days later they rose to 28,000. Ranged at 22,000 until just before death, when they touched 30,000. No autopsy.

22. A. P., æt. 22. Illness lasted 3 days. Left lower lobe involved. Temperature ranged steadily at 103° until death. Leucocytes 50,000 on admission; fell steadily, being 20,000 when death occurred. Autopsy showed beside a double lobar pneumonia, an acute nephritis and fatty degeneration of heart muscle, together with hemorrhage into pericardial sac, with the presence of dip. pneumoniæ.

Of these twenty-two cases, twelve recovered and ten died. Of the twelve favorable cases, four ended by lysis and eight by crisis.

Taking up first the four cases ending by lysis, we see that in all there was a marked leucocytosis at some period of the disease. Examination of the combined leucocyte and temperature charts showed that before the temperature began to fall there was no daily correspondence between the two curves. In all four cases the two curves began to fall together, the leucocytes not reaching normal until one, four and fourteen days after the temperature in cases 1, 2 and 3 respectively. In case 3 there was delayed resolution of the consolidation, it not having entirely cleared up on discharge.

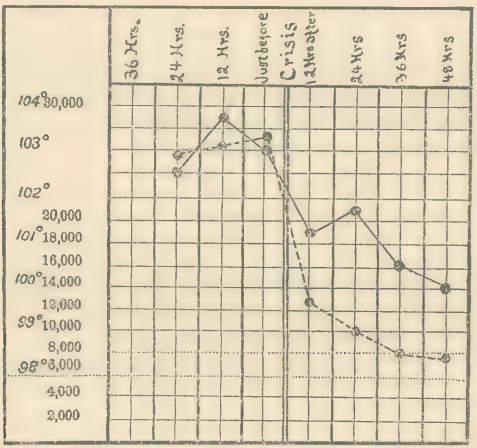
In cases 1 and 3 the leucocytes reached their maximum during the period of fall of temperature. There was a sharp rise during that period in case 3, but the maximum had been reached before the temperature began to fall.

In case 1, where there was involvement of both lungs, the leucocytes reached 50,000. In the other three cases the lower portion of the right lung was involved and the range of the

leucocyte curves was moderate, being above 30,000 in only one instance.

In cases 1, 2 and 4 the fall in temperature preceded the fall of leucocytes.

Case 4 is interesting on account of its complication with rheumatism. The combined chart is given and it shows well the correspondence of the two curves. The occurrence of a moderate leucocytosis during the course of rheumatic fever has been mentioned by several observers. In cases 1 and 2 the leucocytes were 39,500 and 42,000 6 and 8 hours after the chill, respectively.



Black = leucocytes. *Broken = temperature.*

CHART SHOWING TEMPERATURE AND LEUCOCYTE CURVES OF PNEUMONIA. CRISIS.

Of the eight cases ending by crisis, in all but one there was a marked leucocytosis during the febrile period of the disease. In the remaining case the leucocytes, while ranging at normal during the greater period of the disease, touched 13,000 on one occasion. [Case 7.] Examination of the combined charts showed no daily correspondence of the two curves before crisis occurred. The leucocytes began to fall before the temperature in three cases, with it in two, and after it in three. The fall of leucocytes was only partial in six cases, however, and they did not reach normal until from two to eight days after

the temperature. In cases 6 and 7 the leucocytes and temperature reached normal at the same time. In cases 7, 9, 11 and 12 the leucocytes reached their maximum during the period of fall of temperature. In cases 5 and 8 there was a rise of leucocytes during that period, but the maximum had been previously attained. Most of these points are well shown in a combined chart of the eight cases, showing the average temperature and number of leucocytes, twelve, twenty-four and thirty-six hours before and after the crisis in temperature.

In case 9 the lower portions of both lobes were involved and the leucocytes touched the highest point reached in any of the cases, viz., 68,000. In case 11 however, where there was the same extent of involvement, the leucocytes only reached 29,000. In case 7 only the left upper lobe was involved and the leucocyte range was practically normal, only once being above 10,000. The prognosis in this case was thought to be grave at first on account of the absence of leucocytosis, the position of the consolidation, the alcoholic history and patient's age. The patient made an uninterrupted recovery however, and the infection was evidently a very mild one. In the other five cases only a portion of one lung was involved and the leucocyte curve ranged moderately high.

In only one of the eight cases was it possible to count the blood before and after the chill. This was case 9, in which the pneumonia came on while patient was being treated for malarial fever of the double tertian type. In the article on the leucocytes in malarial fever, previously referred to, the fact is brought out that in malarial fever the leucocytes range constantly below normal during the course of the disease. This is due in some way to the presence of the malarial organism in the blood. It is not settled as to whether it is a leukocytolysis (an actual destruction of leucocytes) or a leukopenia (a diminished production). Now in case 9 there was no leucocytosis either before or after the chill, until the exhibition of quinine caused the disappearance of the malarial organisms from the blood, when the leucocytes promptly rose. It is interesting to note how, as each new portion of the lung was involved, there was a corresponding rise in the number of the leucocytes. [See chart.]

Of the ten fatal cases only one (No. 20) showed a complete absence of leucocytosis during the entire course of the disease. In cases 16 and 19 the leucocytes, while being always above normal, ranged relatively low, never being above 19,000. In case 14 the leucocytes behaved as one would expect them to in an uncomplicated case ending in recovery. In cases 15, 17 and 21 the leucocytes were practically normal on admission, but gradually rose during the ensuing three or four days, touching just before death 30,000, 32,000 and 30,000 respectively. In cases 13 and 22 the leucocytes were high on admission, but fell steadily from that time on until death. In case 18 they were normal for the first two days, but rose sharply to 20,000 24 hours before death, falling slightly just before the end.

Thus we see that in fatal cases the behavior of the leucocytes varies widely. In six cases there was absence of leucocytosis at some period of the disease, but the continuous absence is the exception, not the rule. In none of the cases was there any daily correspondence between the temperature and leucocyte curves. In the four cases in which the leucocytes rose at the end however, there was a corresponding rise in temperature. As regards the relation of the amount of leucocytosis to the extent of lung involvement, no definite conclusions can be drawn. In case 15, where the entire right lung and a portion of the left were involved, the maximum leucocytosis was only 30,000 just before death. None of the cases were seen until at least twenty-four hours after the chill, so that no data are furnished as to how early the leucocytosis appears.

Autopsies were obtainable in only three out of the ten cases. This does not include the coroner's inquest on case 19. The results of these autopsies bear out Tchistovitch's statements however. In case 14, where the leucocytes ranged above 20,000, an acute fibrino-purulent meningitis was found to be present. In case 15, where the leucocytes ranged from 17,000 to 30,000 for 5 days, extensive involvement of both lungs was found. In case 22, where the leucocytes ranged from 50,000 to 20,000, there was found at autopsy double lobar pneumonia, acute nephritis, fatty degeneration of the heart muscle, and hæmorrhage into the pericardial sac, with the presence of the

diplococcus pneumoniæ in the latter situation. In case 19, where the leucocytes ranged at 18,000, the fracture of the spine was probably the immediate cause of death. In case 21 there was involvement of both lungs, with a leucocyte range above 20,000. All the remaining cases, with the exception of No. 13, showed a low range of leucocytes, and it is only fair to consider it possible that in case 13 also, an autopsy might have revealed some complication or condition accounting for the relatively high leucocytosis.

There are a number of theories as to the cause of leucocytosis. Virchow held that it was due to proliferation within the lymph glands, that it only occurred in those cases of disease associated with glandular enlargement; also that acute glandular enlargement was followed by leucocytosis. This is negatived by the absence of leucocytosis in many diseases accompanied by glandular enlargement (tuberculosis, acute Hodgkin's disease, etc.), and by the presence of marked leucocytosis in diseases associated with very slight glandular enlargement. [Pneumonia.] Every leucocytosis is probably associated with some glandular enlargement however. Such a leucocytosis as Virchow supposes would be a lymphocytosis, which is not the case.

Schulz's theory has been already mentioned. Its falsity would seem to be proved by the work of Goldscheider and Jacob (to be referred to later), who found that in cases showing a leucocytosis in the peripheral circulation, there was no corresponding diminution in the leucocytes in the central blood-vessels.

Römer (l. c.) thinks the increase due to direct multiplication (by amitosis) of the leucocytes, the exciting cause of such multiplication being the destruction-products of the alkali-proteins, as has been mentioned. He thinks chemotaxis plays a large part. No such changes as he infers are to be made out in the blood.

Von Limbeck (l. c.) holds leucocytosis to be due to the action ("Fernwirkung") of the bacterial products themselves upon the leucocytes. He does not speculate as to the source from which the increase is drawn.

Bieganski's theory has been mentioned. Too little is known about the so-called blood-plates and eosinophiles to justify us

in drawing conclusions from any variations in their number. Most authorities deny that the blood-plates are end-products of the polynuclear leucocytes.

Löwit[23] holds that every leucocytosis is preceded by a diminution in the number of leucocytes. This is due, he thinks, to an actual destruction of the leucocytes, and he calls it leukolysis. This leukolysis is in turn followed by a pouring forth of young elements from the hæmatopoietic organs. This reparation far exceeds the destruction, in this way bringing about a leucocytosis. He demonstrates by injection experiments that the artificially-produced leucocytosis is preceded by a leukolysis. His ideas as to the source from which the increase is drawn would seem to be negatived by the absence of evidence of new formation. Were new formation to occur, the blood would show a large number of young elements. This it does not do.

The latest work on the subject is that of Goldscheider and Jacob[24]. They make use of the terms hypo- and hyperleucocytosis for leukolysis and leucocytosis respectively. Their conclusions are as follows: Hypoleucocytosis is due to the leucocytes being driven into and detained within the capillaries of certain organs of the body. Actual destruction plays a minor rôle. Hyperleucocytosis is due to an increased quantity of leucocytes being carried to the blood by the lymph stream. There is no new formation of leucocytes, its absence being offset by the supposition that in the bone-marrow and spleen there are a large number of adult leucocytes held in reserve, as it were, which are carried off by the lymph stream into the general circulation when occasion arises. The occurrence of new formation is negatived by the absence of young forms in dried specimens.

All these phenomena are primarily due to the bacterial products or chemical substances in the blood. In most acute infectious diseases these substances are introduced into the circulation slowly and cause no diminution in number of the leucocytes, the latter rising immediately. This statement is borne out by experiment. This would mean that in pneumonia the leucocytosis would be found to be present at the time of the chill.

The authors are led to believe that the sources of the leucocytosis are the blood-making organs. But there is no evidence of new formation; hence their theory of a reserve force of adult leucocytes within those organs. This theory seems rather to be constructed to meet the necessity of the case than to be founded on sufficient evidence.

Sherrington[25] in a recent article reports observations of his own on inflammatory leucocytosis. He discusses most of the prevailing ideas, but formulates no new theory.

It is beyond the province of this article to enter into any further discussion of these theories. All we can say is that the leucocytosis in pneumonia is probably due in some way to the products of the diplococcus pneumoniæ. While the bacteria do not enter the blood as a rule, their products do, and in this way can influence the various organs of the body. There is probably no new formation of leucocytes, or at any rate it plays a minor rôle in the process, and some other source for the increase in number of the leucocytes must be sought for.

The behavior of the leucocytes depends upon the virulence of the bacterial products. In fatal cases where the virulence is great, a rise in the number of leucocytes is rendered impossible. It is doubtful whether there is any actual diminution of their number, there being no evidence that actual destruction of leucocytes takes place. The virulence may be so modified as to permit of a gradual increase in number of the leucocytes, yet still be potent to cause death. Cases may begin favorably and the leucocytes may range high at first; the virulence of the bacterial products may then increase, causing a gradual reduction of the leucocytes, and death. The sharp rises sometimes observed just before death may be associated in some way with the pre-agonal leucocytoses. We must not forget that the disease may be present in so mild a form that the leucocytes are unaffected and remain normal throughout. This is shown in case 7 of our series. Most of the above points are shown in the following table:

1. Very mild infection: No effect on leucocytes. Normal range.

2. Moderate infection: Moderate leucocytosis.

3. Severe infection (as to extent of lung involvement): Marked leucocytosis.

4. Severe infection (as to virulence of bacterial product): Moderate leucocytosis.

5. Very severe infection: No leucocytosis.

It has not been proved, as will be shown later, that the blood condition in the fatal cases differs in any way from the normal as regards the relative numerical proportions of the various forms of leucocytes.

If this be true, it is easy to see that the examination of the blood in pneumonia is not of absolute prognostic value. The blood only furnishes an indication of the virulence of the bacterial products; the extent of lung involvement, the general condition of the patient, and the temperature must also be taken into account in every case. For instance, should we be guided by the blood condition alone, our prognosis in cases coming under the heads of 1 and 5 in the above table would be either favorable or unfavorable according to the view we took. The error would of course be fatal.

The absence of leucocytosis in the fatal cases is evidently not the cause of death. Hence the failure of Von Jaksch's treatment by injecting such substances as would produce a leucocytosis in the healthy individual.

Regarding the question of the variations of the different forms of leucocytes, too much time was taken up by the actual counting to allow of much work in this direction. Twenty counts were made in the various cases showing a marked leucocytosis, with the following average result: Polynuclears, 91.2 per cent.; mononuclears, 9.6 per cent.; eosinophiles, 0.2 per cent. Three counts were made in cases showing no leucocytosis, and the results were practically those which would have been obtained in counting the leucocytes in normal blood, thus agreeing with neither Rieder nor Bieganski.

	Polynuclears.	Mononuclears.	Eosinophiles.
(*a*)	71.8 per cent.	28.2 per cent.	0
(*b*)	73.5	26.1	0.4 per cent.
(*c*)	76.1	23.4	0.5

Count (*c*) was in case 18. As has been mentioned, the leucocytes rose sharply just before death. A count was made two hours before death and the increase was found to be in the polynuclears solely. Polynuclears, 95.4 per cent.; mononuclears, 4.3 per cent.; eosinophiles, 0.3 per cent.

These counts would seem to make it doubtful that Bieganski's conclusions hold. The number of counts however, is too small to have any weight.

Conclusions.

1. In cases of pneumonia pursuing a favorable course there is, as a rule, a marked increase in the number of the leucocytes during the febrile period of the disease. This leucocytosis is probably present at the time of the chill, and may be very marked within a few hours. There is no correspondence between the daily temperature and leucocyte curves during the febrile period.

2. In those cases in which the temperature curve falls by crisis, the leucocyte curve begins to fall within a few hours of the same time. The fall of the latter is only partial however, and rarely reaches normal as soon as the temperature curve, generally taking about 48 hours longer. In cases ending by lysis the two curves fall together, the temperature always reaching normal first. In cases of delayed resolution the leucocytes may remain elevated for days.

3. In a majority of the cases the leucocyte curve rises during the period of fall of temperature, and may reach its maximum at that time. Such a rise is only transient, however, and is soon followed by a fresh fall.

4. In cases showing extensive involvement of both lungs, the leucocytes are apt to reach a higher point than in those cases where the involvement is only moderate. The correspondence of lung involvement and amount of leucocytosis is a very rough one however.

5. The fatal cases may show either the presence or absence of leucocytosis. In those cases showing a leucocytosis, some other cause of death than the virulence of the bacterial poison must be sought for.

6. The prognosis in cases showing a complete and continuous absence of leucocytosis is unfavorable as a rule. A continuous absence of leucocytosis is the exception, most cases showing a leucocytosis at some period of the disease. The possibility of the absence of leucocytosis being due to extreme mildness of the disease must not be overlooked.

7. The leucocytosis in pneumonia is a so-called pure leucocytosis, *i. e.* an increase in the polynuclear elements solely. In cases showing no leucocytosis, the blood condition according to the observations here reported, is normal. Further investigations are necessary before the work of previous observers can be positively contradicted.

8. The presence or absence of leucocytosis only shows the virulence of the bacterial poison. It is not a criterion of absolute prognosis.

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